DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Cincinnati District Office
Central Region
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Cincinnati, OH 45237-3097
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November 17, 2003

WARNING LETTER
CIN-04-18828

VIA FEDERAL EXPRESS

Robert H. Douglas, Ph.D.
BET Pharm LLC
1222 Richmond Road
Lexington, KY 40502

Dear Dr. Douglas:

During an inspection of your facility at 1517 Nicholasville Road, Lexington, KY 40503 on June 30, July 1-3, 7, 8, 24, 28, 30 and August 1 and 6, 2003, our investigators observed serious violations of the Federal Food, Drug, and Cosmetic Act (the Act).

Your firm purports to be a compounding pharmacy for veterinary drugs. However, our investigation has determined that your firm exceeds the scope of the regular course of the practice of pharmacy. Your firm's activities go beyond that of a pharmacy and into the activities of a drug manufacturer. Our observations include the following:

1. You repeatedly manufacture Deslorelin, Progesterone P4 LA, Fluprostenol, GnRH injection products, and Fenbenazol and Ivermectin flavored granules from bulk pharmaceutical chemicals and these drugs are used for situations where the health of the animal is not threatened [21 CFR § 530.13(a)].

2. You manufacture the above drug products in commercial size lots in anticipation of receiving prescriptions [21 CFR § 530.13(b)(5)]. For example, you have compounded [redacted] lots of Deslorelin Injection, 1.5 mg/ml from bulk deslorelin between January 1 and June 30, 2003; and you have compounded [redacted] lots of Progesterone Injection, 150 mg/ml from bulk chemical progesterone, USP between August 1, 2002 and June 30, 2003. There were still [redacted] units of Deslorelin Injection 1.5 mg/ml of

lot 04232003@6 in your inventory at the conclusion of the FDA inspection.

3. You are compounding drugs for use in animals where an approved new animal drug used as labeled will, in available dosage form and concentration, appropriately treat the condition diagnosed [21 CFR § 530.13(b)(2)]. For example, there is an approved NADA for implantable deslorelin, which will appropriately induce ovulation.

4. Your firm is not filling prescriptions within the confines of a valid Veterinarian-Client-Patient Relationship in that: the drug products compounded from August 2002 to May 2003 were compounded by individuals who are not licensed pharmacists or veterinarians; the prescription orders (order forms) fail to record critical information necessary to establish a medical need for a specific patient; and the labels bear expiration dates which are a set period of time rather than the veterinarian's treatment period [21 CFR § 530.13(b)(1) and (b)(3)].

In light of the above, your firm is not operating as a pharmacy engaged in extemporaneous compounding. The only legal compounding of animal drugs is provided under the Animal Medicinal Drug Use Clarification Act and its implementing regulations at 21 CFR Part 530, Extralabel Drug Use in Animals. Our investigation found that you did not comply with these requirements. For example, 21 CFR 530.13(a) requires that the compounding be conducted using approved animal or human drug products. However, your firm compounded with the use of bulk active pharmaceutical ingredients, which is not permitted. In addition, the compounded drug products were not labeled with directions for use specified by the veterinarian, including the animal or animals in which the drug is intended to be used, as required by 21 CFR 530.12(c). The veterinary drugs compounded and distributed by your firm are new animal drugs within the meaning of section 201(v) of the Act (21 U.S.C. § 321(v)). These drugs are adulterated under section 501(a)(5) of the Act (21 U.S.C. § 351(a)(5)) because they are unsafe within the meaning of section 512 of the Act (21 U.S.C. § 360b). Under section 512, a new animal drug is deemed to be unsafe unless an approved New Animal Drug Application (NADA) is in effect for the specific product in question. None of the animal drugs compounded and distributed by your firm are the subject of an approved NADA.

As a manufacturer of animal drugs, the Act also imposes other requirements on your firm. During the inspection of your firm, our investigator observed other violations of the Act. For instance, your drug products are misbranded under section 502(f)(1) of the Act (21 U.S.C. § 352) in that their labeling fails to bear adequate directions for use and they are not exempt from this requirement under 21 CFR § 201.115 because they are unapproved new animal drugs. In addition, your drug products are misbranded under section 502(o) of the Act (21 U.S.C. § 352(o)) because they are manufactured in an established not duly registered under section 510 (21 U.S.C. § 360), and the drug products have not been listed as required under section 510(j)(21 U.S.C. § 360(j)). Your facility is not exempt from the registration and listing requirements under section 510(g) of the Act (21 U.S.C. 360(g)) and 21 CFR § 207.10.

Your drug products are also adulterated within the meaning of section 501(a)(2)(B) of the Act (21 U.S.C. § 351(a)(2)(B)) in that the controls and procedures used to manufacture, process, pack, and hold them do not conform to current good manufacturing practice. The deviations observed by our investigator include, but are not limited to the following:

1. There is no Quality Control unit [21 CFR § 211.22].

2. There is no testing of the finished product lots to assure identity and strength of the active ingredients prior to release [21 CFR § 211.165(a)].

3. There are no records to show that the sterile drug products have been sterility tested, and the sterility test utilized has not been validated for use for injectable drugs [21 CFR § 211.167(a)].

4. There are no written procedures for cleaning and maintaining manufacturing equipment to assure there is no cross contamination [21 CFR § 211.67(a)]. For example, deslorelin and progesterone are both dispensed using the same [redacted].

5. No scientifically based specifications have been established for the drug products [21 CFR § 211.160(b)].

6. There is no stability data to support the expiration periods assigned to the drug products [21 CFR § 211.166].

7. There is no testing performed for excipients or active drug substances prior to use in drug products [21 CFR § 211.84(a)].

8. There are no written procedures for production and process controls [21 CFR § 211.100(a)].

9. There are no written procedures for handling drug product complaints and the record of complaints and investigations were not available for review [21 CFR § 211.198].

10. The prescription distribution records are not accurate for all lots and the distribution of those lots could not be readily determined in the event of a recall [21 CFR § 211.196].

11. The batch records and formula worksheets are incomplete and inconsistent [21 CFR § 211.188].

The above is not intended to be an all-inclusive list of violations by your firm. As a manufacturer of animal drugs, you are responsible for ensuring that your operations and your drug products are in compliance with the Act and its implementing regulations. Failure to promptly correct these violations may result in regulatory action being initiated by FDA without further notice. Possible actions include, but are not limited to, seizure and/or injunction.

Within fifteen (15) working days of receiving this letter, please notify this office in writing of the specific steps you have taken to correct these deficiencies. If corrective action cannot be completed within fifteen (15) working days, state the reason for the delay and the timeframe within which the corrections will be completed.

Your written response to this Warning Letter should be sent to Ms. Gina Brackett, Compliance Officer, Food and Drug Administration, 6751 Steger Drive, Cincinnati, Ohio 45237. If you have any questions concerning this letter, you may contact Ms. Brackett at (513) 679-2700, extension 167, or you may forward a facsimile to her at (513) 679-2773.

Sincerely,

for

Carol A. Heppe
District Director
Cincinnati District